

Liver Cell Transplantation

Grant Award Details

Liver Cell Transplantation

Grant Type: Early Translational II

Grant Number: TR2-01857

Project Objective: develop hESC derived hepatocyte like cells, hEDH, for the treatment of acute liver failure induced by surgical resections.

Investigator:

Name: Mark Zern

Institution: University of California, Davis

Type: PI

Name: Holger Willenbring

Institution: University of California, San Francisco

Type: Co-PI

Disease Focus: Liver Disease

Human Stem Cell Use: Embryonic Stem Cell

Award Value: \$4,212,621

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

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Grant Application Details

Application Title: Liver Cell Transplantation

Public Abstract: Because there is still considerable morbidity and mortality associated with the process of whole liver transplantation, and because more than a thousand people die each year while on the liver transplantation list, and tens of thousands more never get on the list because of the lack of available livers, it is evident that improved and safer liver transplantation would be valuable, as would approaches that provide for an increased number of transplantations in a timely manner. A technology that might address these issues is the development of a human liver cell line that can be employed in liver cell transplantation or in a bioartificial liver. Developing such a cell line from human embryonic stem cells (hESC) would provide a valuable tool for pharmacology studies, as well as for use in cell-based therapeutics. The objective of this proposal is to focus a team effort to determine which differentiated hESC will be the most effective liver-like cells in cell culture and in animal studies, and to then use the best cells in clinical trials of cell transplantation in patients with advanced liver disease.

In the proposed studies, the team will differentiate hESC so that they act like liver cells in culture. Once it has been established that the cells are acting like liver cells by producing normal human liver proteins, and that they do not result in tumors, the cells will be assessed in clinically-relevant models using techniques that can then be adapted to future human clinical trials. One of the ways cells can be evaluated is to label the cells which will provide a means to monitor them with various imaging systems. The intent in these studies is to determine which will be the most effective cells to use in human clinical trials. Once this is determined, the best cells can then be employed in human patients.

If the studies are successfully undertaken, we will have established a clinically useful and viable liver cell line that could be used to repopulate an injured liver in a safer and less expensive manner than with whole liver transplantation. Moreover, all people who have liver failure or an inherited liver disease could be treated, because there would be an unlimited supply of liver cells.

Statement of Benefit to California: In California, as in all parts of the US, there are not enough livers available for transplantation for all the people who need them. The result is that many more people die of liver failure than is necessary. One way to improve this situation is the transplantation of liver cells rather than whole organ transplantation. We are attempting to develop liver cell lines from stem cells that will act like normal liver cells. If the cells that we develop function well and do not act like cancer cells in culture, the cells will be assessed in clinically-relevant models using techniques that can then be adapted to future human clinical trials. In our studies, we will compare human embryonic stem cells with other stem cells to determine which will be the most effective cells to transplant into people. In the future, we will employ the best cells in clinical trials in humans. If the studies are successfully undertaken, we will have established a clinically useful and viable liver cell line that could be used to repopulate an injured liver in a safer and less expensive manner than with whole liver transplantation. Moreover, all people who have liver failure or an inherited liver disease could be treated, because there would be an unlimited supply of liver cells.